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INCYTE CORPORATION
3160 PORTER DRIVE
PALO ALTO, CA 94304

EXAMINER	
FRONDA, CHRISTIAN L	
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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Paper No. 20040517

Application Number: 09/830,914
Filing Date: May 02, 2001
Appellant(s): TANG ET AL.

James M. Verna
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed March 09, 2004.

(1) Real Party in Interest

A statement identifying the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

A statement identifying the related appeals and interferences which will directly affect or be directly affected by or have a bearing on the decision in the pending appeal is contained in the brief.

(3) Status of Claims

The statement of the status of the claims contained in the brief is correct.

(4) Status of Amendments After Final

The amendment after final rejection filed on December 4, 2003 has not been entered.

(5) Summary of Invention

The summary of invention contained in the brief is correct.

(6) Issues

The appellant's statement of the issues in the brief is correct.

(7) Grouping of Claims

Appellant's brief includes a statement that all claims on appeal are grouped together.

(8) Claims Appealed

The copy of the appealed claims contained in the Appendix to the brief is correct.

(9) Prior Art of Record

Attwood et al. Which craft is best in bioinformatics? Comput. Chem. 2001, Vol. 25(4), pp.329-339.

Ponting, C.P. Issues in predicting protein function from sequence. Brief. Bioinform. March 2001, Vol. 2(1), pp. 19-29.

(10) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

35 U.S.C. § 101

Claims 23-31 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a credible, specific and substantial asserted utility or a well established utility.

The specification discloses the nucleotide sequences of SEQ ID NO: 2, the deduced amino acid sequence of the protein encoded as SEQ ID NO: 1, and assigned the protein of SEQ ID NO: 1 as a "new human myosin heavy chain homology (MHCH)" based on homology to myosin proteins known in the prior art. (see p. 17, lines 15 to p. 18, line 11 of the specification). However, the specification does not disclose the specific function of the protein of SEQ ID NO: 1 or its specific relationship to any disease. The specification does not disclose any activity assays to demonstrate that the protein encoded by the polynucleotide of SEQ ID NO: 2 has any biological activity. Homology is not a disclosure of how to use the claimed polynucleotide and protein. While the claimed invention can be used in gene and protein expression monitoring experimentations, the specification does not teach any meaningful interpretation of data

collected from such experimentations. Nor does the specification teach how to use any identified compound which modulates the expression of the claimed invention.

Substantial utility is one that provides a specific benefit in currently available form at the time of filing of the invention. However, the main utility of the nucleic acid and protein is to carry out further research to identify the biological function and possible diseases associated with the nucleic acid and protein. Utilities that require or constitute carrying out further research to identify or reasonably confirm a specific use are not substantial utility and do not provide a specific benefit. Thus, the claimed invention has no credible, specific and substantial asserted utility or well established utility.

35 U.S.C. § 112, 1st Paragraph - Enablement

Claims 23-31 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a credible, specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Furthermore, claims 23, 26, 27, 28, and 30 which encompass any polynucleotide of any nucleotide sequence encoding a polypeptide having an amino acid sequence that is at least 90% identical to SEQ ID NO: 1 wherein said polypeptide has ATPase activity, and any polynucleotide having 70% identity to SEQ ID NO: 2 are not enabled by the specification.

Factors to be considered in determining whether undue experimentation is required, are summarized In re Wands [858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)]. The Wands factors are: (a) the quantity of experimentation necessary, (b) the amount of direction or guidance presented, (c) the presence or absence of working example, (d) the nature of the invention, (e) the state of the prior art, (f) the relative skill of those in the art, (g) the predictability or unpredictability of the art, and (h) the breadth of the claim.

The nature and breadth of the claims 23, 26, 27, 28, and 30 encompass any polynucleotide of any nucleotide sequence encoding a polypeptide having an amino acid sequence that is at least 90% identical to SEQ ID NO: 1 wherein said polypeptide has ATPase activity, and any polynucleotide having 70% identity to SEQ ID NO: 2

The specification provides guidance and examples for making an isolated polynucleotide encoding a polypeptide comprising the amino acid sequence of SEQ ID NO: 1 or an isolated polynucleotide comprising SEQ ID NO: 2. However, the specification does not teach the specific structural/catalytic amino acids and the structural motifs essential for protein activity/function which cannot be altered.

The state of the art as exemplified by Attwood et al. (Comput. Chem. 2001, Vol. 25(4), pp. 329-39) is such that "...we do not fully understand the rules of protein folding, so we cannot predict protein structure; and we cannot invariably diagnose protein function, given knowledge only of its sequence or structure in isolation" (see Abstract and entire publication). Furthermore, Ponting (Brief. Bioinform. March 2001, Vol. 2(1), pp. 19-29) states that "...predicting function by homology is a qualitative, rather than

quantitative, process and requires particular care to be taken...due attention should be paid to all available clues to function, including orthologue identification, conservation of particular residue types, and the co-occurrence of domains in proteins" (See Abstract and entire publication).

In order to meet the enablement requirement under 35 U.S.C. § 112, 1st Paragraph, one of skill in the art must be able to make the claimed invention without undue experimentation. However, the amount of experimentation to make the claimed polynucleotides is enormous and undue and entails selecting specific nucleotides to change (deletion, insertion, substitution, or combinations thereof) in any polynucleotide to make a polynucleotide of any nucleotide sequence having at least 70% identity to SEQ ID NO: 2 or to make in any polynucleotide of any nucleotide sequence encoding any polypeptide having an amino acid sequence that is at least 90% identical to SEQ ID NO: 1, and determining by assays whether the polypeptide has ATPase activity. The specification does not provide guidance with respect to the specific structural/catalytic amino acids and the structural motifs essential for enzyme structure and activity/function which must be preserved. Thus, searching for the specific nucleotides to change (deletion, insertion, substitution, or combinations thereof) in a polynucleotide to make the claimed polynucleotides is well outside the realm of routine experimentation and predictability in the art of success in determining whether the resulting polypeptide has ATPase activity is extremely low since no information is provided by the specification regarding the specific catalytic amino acids and the structural motifs essential for enzyme structure and activity/function which must be preserved.

The Examiner finds that one skilled in the art would require additional guidance, such as information regarding the specific catalytic amino acids and the structural motifs essential for activity/function which must be preserved. Without such a guidance, the experimentation left to those skilled in the art is undue.

35 U.S.C. § 112, 1st Paragraph - Written Description

Claim 30 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 30 is directed to any polynucleotide of any biological function having 70% identity to SEQ ID NO: 2. The specification, however, only provides the following representative species encompassed by this claim: a polynucleotide consisting of the nucleotide sequence of SEQ ID NO: 2. There is no disclosure of any particular structure to function/activity relationship in the disclosed species. The specification also fails to describe additional representative species of the claimed polynucleotides having 70% identity to SEQ ID NO: 2.by any identifying structural characteristics or properties for which no predictability of structure is apparent. Given this lack of additional representative species as encompassed by the claims, Appellants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Appellants were in possession of the claimed invention.

(11) Response to Argument

Beginning on page 4, last paragraph of the Brief, Appellants state that the inventions is a polynucleotide of SEQ ID NO: 2 that is expressed in human tissues and codes for a protein having the deduced amino acid sequence of SEQ ID NO: 1, where the protein is assigned as a "new human myosin heavy chain homolog (MHCH)" (see p. 17, lines 15-18 of the specification). Appellants assert that there are similarities between the invention of SEQ ID NO: 1 and C.elegans myosin (g1279777) and H.annuus unconventional myosin (g2444174) and that by sequence homology analysis that the claimed invention of SEQ ID NO: 1 has various structural motifs including myosin head domain, myosin heavy chain and light chain binding sites (see page 17, line 30 through page 18, line 9 of the specification).

Appellants argue on pages 14-15 of the Brief, that the protein encoded by the claimed polynucleotide is a member of the myosin family and that the Examiner has not provided sufficient evidence or reasoning to the contrary. Appellants argue on pages 16-17 of the Brief that the precise biological role or function of an expressed polynucleotide is not required to demonstrate utility. Appellants argue on pages 17-19 of the Brief that membership in a class of useful products can be proof of utility

Appellants' arguments have been fully considered but are not persuasive for several reasons. While the Examiner agrees with Appellants that the myosin family of proteins is diverse and of members of the myosin family have been shown to have specific biological functions in the prior art, the Examiner disagrees with Appellants assertion that the claimed polynucleotide of SEQ ID NO: 2 encodes a protein that is a

member of the myosin family of proteins and with Appellants assertion that the precise biological role or function of an expressed polynucleotide is not required to demonstrate utility.

The specification does not disclose that the claimed polynucleotide of SEQ ID NO: 2 is a marker for a specific disease(s). There is no disclosure of altered levels or forms of the polynucleotide of SEQ ID NO: 2 in any diseased tissue compared to healthy tissue. Thus, the polynucleotide of SEQ ID NO: 2 is not a disease marker or appropriate target for drug discovery or toxicology testing.

The state of the art as exemplified by Attwood et al. (Comput. Chem. 2001, Vol. 25(4), pp. 329-39) is such that "...we do not fully understand the rules of protein folding, so we cannot predict protein structure; and we cannot invariably diagnose protein function, given knowledge only of its sequence or structure in isolation" (see Abstract and entire publication). Furthermore, Ponting (Brief. Bioinform. March 2001, Vol. 2(1), pp. 19-29) states that "...predicting function by homology is a qualitative, rather than quantitative, process and requires particular care to be taken...due attention should be paid to all available clues to function, including orthologue identification, conservation of particular residue types, and the co-occurrence of domains in proteins" (See Abstract and entire publication).

The specification does not disclose the specific function of the protein of SEQ ID NO: 2. On page 18, line 6 of the specification, the amino acid sequences of MHCH and myosin I heavy chain only share 23.2% sequence identity. Furthermore, on page 18,

lines 7-8, the amino acid sequences of MHCH and unconventional myosin I share only 22.4% sequence identity.

The specification does not explicitly state that homology to known proteins in the prior art is a disclosure that the claimed invention automatically has the biological function and activity of the prior art proteins relied upon. Furthermore, homology to known proteins in the prior art is not a disclosure of how to use the polynucleotide of SEQ ID NO:2 or the encoded polypeptide of SEQ ID NO: 1. No further information is provide by the specification regarding the specific activity and function of the claimed polynucleotide other than the encoded protein is a "new human myosin heavy chain homolog (MHCH)" (see p. 17, lines 15-18 of the specification).

Hence, in view of the teachings of Attwood et al. (Comput. Chem. 2001, Vol. 25(4), pp. 329-39) and Ponting (Brief. Bioinform. March 2001, Vol. 2(1), pp. 19-29) and in view of the amino acid sequences of MHCH and myosin I heavy chain sharing only 23.2% sequence identity and the amino acid sequences of MHCH and unconventional myosin I sharing only 22.4% sequence identity, one skilled in the art cannot conclude that the claimed polynucleotide of SEQ ID NO:2 encodes a protein that is a member of the myosin family.

Furthermore, citing Brenner V. Manson 148 USPQ at 696, "Congress intended that no patent be granted on a chemical compound whose sole 'utility' consists of it potential role as an object of use-testing." It appears that the main utility of the claimed nucleic acid and protein is to carry out further research to identify the biological function of the claimed nucleic acid and protein.

Appellants argue beginning on page 5 of the Brief that the claimed invention has many uses including toxicology testing, drug development, and diagnosis of disease. Appellants assert on page 5, lines 6-9, that the stated uses does not require "knowledge of how the polypeptide coded for by the polynucleotide actually functions".

Appellants discuss the Bedilion Declaration previously submitted on July 7, 2003. It should be noted that Dr, Bedilion is a consultant for Incyte Pharmaceuticals, Inc., the real party in interest in this appeal, and thus is a concerned party. Appellants quote from the Bedilion declaration that microarrays containing polynucleotides encoding SEQ ID NO: 2 would be a more useful tool than microarrays lacking these polynucleotides in conducting gene expression monitoring studies on proposed or actual drugs for treating various diseases and/or disorders. Appellants argue that the claimed polynucleotide can be used as a probe for in gene expression monitoring applications.

This is not found to be persuasive because any new polynucleotide can be used in microarray applications, and thus this asserted utility is not specific. The specification does not disclose that the claimed polynucleotide has altered levels or forms of the polynucleotide of SEQ ID NO: 2 in any diseased tissue compared to healthy tissue. Thus, it cannot be concluded that the polynucleotide of SEQ ID NO: 2 is an appropriate target for drug discovery or toxicology testing. While the claimed invention can be used in gene expression monitoring experimentations, the specification does not teach any meaningful interpretation of data collected from such experimentations, and thus this asserted utility is not substantial.

On page 5, last paragraph, of the Brief, Appellants argue that the uses of the claimed polynucleotide of SEQ ID NO: 2 instead of the function of the claimed polynucleotide of SEQ ID NO: 2 is the subject of a proper analysis of the utility requirement, and that one of ordinary skill in the art in view of the Bedilion Declaration can attain beneficial results from the claimed polynucleotide despite any having no knowledge of the function of the claimed polynucleotide.

This is not found to be persuasive for several reasons. Appellants mischaracterize the Examiner's positions regarding the utility requirement under 35 U.S.C. § 101. An invention directed toward a new polynucleotide can meet utility requirement under 35 U.S.C. § 101 provided that the specification discloses a credible, specific and substantial asserted utility for the new polynucleotide, or a well-established utility for the claimed polynucleotide. If the specification would have disclosed that the claimed polynucleotide is clearly expressed in a specific disorder or disease such as colon cancer and not expressed in healthy colon tissue, then the polynucleotide would be considered a marker for colon tissue and may not be rejected under 35 U.S.C. § 101 and 35 U.S.C. § 112. However, this is not the case. The instant specification discloses a polynucleotide of SEQ ID NO: 2 and hypothesizes that the claimed polynucleotide encodes a polypeptide involved in cell proliferative and developmental disorders, but the expression of the polynucleotide of SEQ ID NO: 2 in a specific diseased tissue and corresponding healthy tissue was not evaluated.

On pages 6-7 of the Brief, Appellants cite several cases to support Appellants' position that the claimed polynucleotide of SEQ ID NO: 2 has "well-established" uses that are specific and beneficial. Appellants argue on pages 7-12 of the Brief that the invention has utility because of its use in toxicology testing, drug discover, and disease diagnosis which is asserted to confer specific benefits to the public. Appellants assert that it cannot be disputed that the claimed polynucleotide is a useful tool in cDNA microarrays. Appellants argue on pages 12-14 of the Brief, that using nucleic acids coding for proteins for use in toxicology testing, drug discover, and diagnosis of disease is "well -established".

Appellants' arguments have been fully considered but are not deemed to be persuasive. For a utility to be "well-established" it must be specific, substantial, and credible. In the instant case, all nucleic acids and genes are in some combination useful in toxicology testing. However, the particulars of toxicology testing with the claimed polynucleotide is not disclosed in the instant specification. Neither the toxic substances nor the susceptible organ systems are identified. Therefore, this is a utility which would apply to virtually every member or a general class of materials, such as any collection of proteins or DNA, but is only potential with respect to the claimed polynucleotide. Thus, such utility is not specific and does not constitute a "well-established" utility. Further, because any potential diagnostic utility is not yet known and has not yet been disclosed, the utility is not substantial because it is not currently available in practical form.

Appellants argue on pages 15-16 of the Brief that a "real world" utility exists if actual use or commercial success can be shown. Citing case law, Appellants assert that such a showing is conclusive proof of utility. Appellants state that a vibrant market has developed for databases containing all expressed genes including those of Incyte, the real party at interest in the instant appeal. Appellants argue that Incyte's customers and the scientific community have acknowledged that Incyte's databases have proven valuable, and that the databases including the claimed polynucleotide would be even more valuable.

Appellants' arguments have been fully considered but are not deemed to be persuasive. The case law indicates that a rejection under 35 U.S.C. § 101 for lack of operability can be overcome by showing of actual use or commercial success. However, the instant issue is whether or not the asserted utilities are credible, specific, and substantial. This issue is not addressed by showing commercial success or actual use. Evidence of commercial success, while sometimes persuasive as secondary evidence of non-obviousness, is immaterial to utility and enablement. Many products such as pet rocks have enjoyed commercial success due to fads or clever advertising, where the products would not have met the legal standard for utility and enablement.

Appellants argue on pages 19-20 of the Brief the rejection is incorrectly based on grounds that use of an invention as a tool for research is not a substantial use. Appellants assert that only a limited subset of research uses are not substantial: those in which the only known use for the claimed invention is to be an object of further study, thus merely inviting further research.

This is not found to be persuasive since while a microarray or gas chromatograph has patentable utility as a research tool, the objects being evaluated with those research tools do not necessarily have patentable utility. In the instant case, the claimed polynucleotide is not disclosed as having a specific biological activity or having any property that can be specifically useful, such as a differential pattern of expression in a specific diseases tissue. The claimed polynucleotide is in fact an object for further study and further research. None of the asserted utilities for the claimed polynucleotide of SEQ ID NO: 2 meets the three-pronged test of being specific, substantial, and credible.

Appellants argue on pages 20-22 of the Brief that requiring the patent applicant to assert a particular or unique utility, it is alleged that the patent examination utility guidelines and training materials applied by the patent examiner misstate the law. Appellants challenge the legality of the Patent Examination Utility Guidelines. Since the Examiner has no authority to comment on the legality the Patent Examination Utility Guidelines, the issue will be reserved for ruling by the Board of Patent Appeals and Interferences.

Appellants argue on page 22 of the Brief that since the rejection under 35 U.S.C. § 112, 1st Paragraph, is based on an alleged improper rejection for lack of utility under 35 U.S.C. § 101, the rejection under 35 U.S.C. § 112, 1st Paragraph must be reversed.

This not found to be persuasive since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the

claimed invention. Until a specific and substantial utility can be determined for the claimed polynucleotide and polypeptide encoded, one of ordinary skill in the art would be required to perform additional experimentation in order to determine how to use the claimed invention. Thus, there is no immediately apparent or "real world" utility as of the filing date of the instant invention.

On page 23-24 of the Brief, Appellants point out that the claimed invention is directed toward naturally-occurring variants. Appellants cite the case In re Marzocchi, 169 USPQ 367, 369 (CCPA 1971) in which "the first paragraph of § 112 requires nothing more than objective enablement". Appellants argue that it is not necessary to screen every conceivable variant since appellants allege that the claimed invention encompasses variant sequences found in nature and that through natural selection, nature will have determined the appropriate sequences. Appellants argue that sequence analysis methods are well known and that one of ordinary skill in the art could identify without undue experimentation a polynucleotide encoding a polypeptide comprising a naturally occurring amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO: 1 or polynucleotide comprising a naturally occurring nucleotide sequence at least 70% identical to the nucleotide sequence of SEQ ID NO: 2. Appellants state that PCR and hybridization techniques could be used to screen a cDNA library for the claimed polynucleotide that already exists in nature. Appellants argue that the specification provides specific assays for myosin activity,

binding assays, and immunological methods for detecting and measuring MHCH. Appellants argue that the claims are directed toward polynucleotides and not polypeptides encoded by them. Appellants conclude that given this guidance, one of ordinary skill in the art would known how to select and screen for the polynucleotides of the claimed invention without undue experimentation.

On pages 25-26 of the Brief, Appellants argue that the Attwood et al. reference does not suggest that functional homology cannot be inferred by a reasonable probability and that Attwood et al. teach that motifs "effectively provide diagnostic family signatures". Appellants' position is that the specification teaches specific catalytic amino acid residues and structural motifs essential for protein activity, where the encoded polypeptide of the invention is alleged to have a myosin head domain and myosin heavy chain and light chain binding site signatures. Appellants argue that there is no requirement for working examples and that "one looks to whether the specification provides a description of how to make what is claimed".

Appellants' arguments have been fully considered but are not found to be persuasive for several reasons. Appellants' arguments do not address the instant issue of the enablement requirement: the specification must provide guidance to one of ordinary skill in the art on how to make the claimed invention without undue experimentation.

Appellants' arguments that one skilled in the art need not make and test vast numbers of polypeptides and that only screening of cDNA libraries using appropriated PCR or hybridization conditions is required to make the claimed invention are not

persuasive since such guidance is not guidance for making the claimed invention but rather searching and screening for the claimed polynucleotides. Screening and searching for the claimed invention is not guidance for making the claimed invention.

The cited references of Attwood et al. and Ponting provide rational and scientific explanations of the pitfalls in predicting or assigning any biological function base solely on a polynucleotide sequence or a deduced amino acid sequence. As stated above, Attwood et al. teach that "...we do not fully understand the rules of protein folding, so we cannot predict protein structure; and we cannot invariably diagnose protein function, given knowledge only of its sequence or structure in isolation" . Thus, one skilled in the art would be appraised of the difficulties in making the claimed invention.

The specification does not disclose the specific function of the protein of SEQ ID NO: 2. On page 18, line 6 of the specification, the amino acid sequences of MHCH and myosin I heavy chain only share 23.2% sequence identity. Furthermore, on page 18, lines 7-8, the amino acid sequences of MHCH and unconventional myosin I share only 22.4% sequence identity.

The specification does not explicitly state that homology to known proteins in the prior art is a disclosure that the claimed invention automatically has the biological function and activity of the prior art proteins relied upon. Simply assigning parts of the amino acid sequence of SEQ ID NO: 2 as having a myosin head domain and myosin heavy chain and light chain binding site motifs without discussing the fact that more than 80% of the amino acid sequence of SEQ ID NO:2 is different from the amino acid sequences of the cited myosin I heavy chain and unconventional myosin I does not

automatically mean that the claimed invention is a myosin protein. Thus, one of ordinary skill in the art cannot conclude that the claimed polypeptide is a myosin protein having ATPase activity.

SEQ ID NO: 1 of the invention consists of 612 amino acid residues. Claim 23 encompasses any polynucleotide encoding any polypeptide that has an amino acid sequence that is at least 90% identity to SEQ ID NO:1. In order to fall within the scope of claim 23, an amino acid sequence of a polypeptide must have at least 550 amino acid residues that are identical to SEQ ID NO: 1 and no more than 61 amino acid residues that are different from SEQ ID NO: 1. Since three consecutive nucleotide bases constitute a codon specifying an amino acid residue, then no more than 183 nucleotides can be different in a polynucleotide encoding any polypeptide that has an amino acid sequence that is at least 90% identity to SEQ ID NO:1 to fall within the scope of the claim. SEQ ID NO: 2 of the invention consists of 2190 nucleotides. Claim 30 encompasses any polynucleotide that is at least 70% identical to SEQ ID NO: 2. In order to fall within the scope of claim 30, a polynucleotide must have a nucleotide sequence that has at least 1533 nucleotides that are identical to SEQ ID NO: 2 and no more than 438 nucleotides that are different from SEQ ID NO: 2.

The specification, however, does not provide guidance for the specific amino acid residues in SEQ ID NO: 1 which cannot be changed and specific amino acid residues that can be changed in order to preserve ATPase activity. The specification does not teach the specific nucleotides that can be changed and cannot be changed in order to encode a polynucleotide that encodes a polypeptide that still has ATPase activity while

having an amino acid sequence that is 90% identical to SEQ ID NO: 1. The specification does not teach which of the 438 nucleotides of SEQ ID NO:2 can be changed and which of the 1533 nucleotides of SEQ ID NO: 2 cannot be changed.

The recitation of "naturally occurring amino acid sequence" in the claims does not meet the enablement requirement since the specification must still provide guidance regarding the specific amino acid residues in the amino acid sequence of SEQ ID NO: 1 which cannot be changed and amino acid residues which can be changed but still retain ATPase activity.

In order to meet the enablement requirement, the specification must provide guidance as to the specific amino acid residues in the amino acid sequence of SEQ ID NO: 1 which cannot be changed and amino acid residues which can be changed but still retain ATPase activity. However, the specification does not identify within SEQ ID NO: 1 the critical amino acid residues that cannot be changed and which are involved in ATPase activity nor have Appellants identified amino acid residues that can be changed without affecting ATPase activity.

While working examples that show that the claimed invention has ATPase activity are not required, absence of working examples in combination with absence of teachings regarding critical catalytic and structural amino acid residues that cannot be changed and the state of the art exemplified by the teachings of Attwood et al. and Ponting invites an enormous and undue amount of experimentation to make the claimed invention, where such experimentation entails determining the specific biological function of the polynucleotide and protein encoded, determining the specific amino acid

residues critical for protein activity and structure, making polynucleotide and polypeptide variants falling with the scope of claim 23 and 30 by recombinant techniques, and determining whether such variants still retain protein function and activity.

Appellants cite case law beginning on page 27 of the Brief to support Appellants' position that the written description requirement is met by what is specifically disclosed and what is conventional or well known to one skilled in the art. Appellants argue given that the specification discloses SEQ ID NO: 1 and SEQ ID NO: 2, one of ordinary skill in the art would recognize naturally-occurring variants of SEQ ID NO: 1 having 90% sequence identity to SEQ ID NO:1 and naturally-occurring variants of SEQ ID NO: 2 having 70% sequence identity to SEQ ID NO: 2. Appellant thus conclude that the specification provides an adequate written description of the claimed invention.

Appellants argue in pages 28-30 of the Brief that a common basis for which courts have found claims to DNA to be invalid is the recitation of functional properties of a DNA without the definition of structural features of the DNA. Appellants summarize cases Fiers v. Revel, 25 U.S.P.Q.2d 1601, 1606 (Fed. Cir. 1993) and University of California v. Eli Lilly and Co., 43 U.S.P.Q.2d 1398, 1406 (Fed. Cir. 1997). Appellant argue that in contrast to Lily and Fiers cases where nucleic acids that were defined on the basis of functional characteristics alone did not meet the written description requirement of 35 U.S.C. § 112, 1st Paragraph, the claims at issue define the nucleic acid by structure alone rather than on functional characteristics. Appellants conclude

that the Office Action fails to explain how the claims of the instant invention are different from the nucleic acid claims of the Lily and Fiers cases which were found to be invalid.

Appellant argue in page 30 that the present claims do not define a "highly variant" genus. Appellants cite the Brenner et al. reference to demonstrate that the claimed genus is of narrow scope. Appellants state that the Brenner et al. reference teaches an analysis of proteins with known structural and functional relationship indicates that 30% identity over at least 150 amino acid residues between two amino acid sequences is reliable in establishing evolutionary homology and that 40% identity over at least 70 residues is a reliable in "signifying homology between proteins". Appellants thus argue that only myosin proteins having 40% identity over at least 70 residues of SEQ ID NO: 1 instead of all potential myosin proteins "related to SEQ ID NO: 1" would be encompassed by the claimed genus.

Appellants argue on page 31 that the state of the art has advanced since the time of filing of the cited cases of Lilly and Fiers and the present application. Appellants cite the invention of polymerase chain reaction (PCR), efficient cloning and sequencing of DNA, and compilation of large protein and nucleotide sequence databases. Appellants conclude that one of skill in the art would recognize given the amino acid sequence of SEQ ID NO: 1 and the amino acid sequence of SEQ ID NO: 2 that the inventors were in possession of the claimed invention.

Appellants' arguments have been fully considered and are found to be persuasive for withdrawing the written description rejection on claims 23, 26-28, and 31.

However, the written description rejection on claim 30 is maintained for the following reasons.

A review of the language of claim 30 indicates that the claimed invention is drawn to a genus of polynucleotides with widely differing structural, chemical, and physical characteristics. The genus is highly variable because a significant number of structural differences between genus members is permitted as evident by the recitation that the claimed polynucleotides have a nucleotide sequence that is at least 70% identical to the nucleotide sequence of SEQ ID NO: 2. The claimed genus encompasses a wide breadth of polynucleotides with widely differing biological functions such as encoding widely differing proteins and enzymes. Furthermore, the claimed genus encompasses polynucleotides with biological functions that have yet to be discovered.

Appellants' argument that the explicit disclosure of the amino acid sequence of SEQ ID NO:1 and the nucleotide sequence of SEQ ID NO: 2 is sufficient to meet the written description requirement is not persuasive since the genus is highly variable and encompasses a wide breadth of polynucleotides with widely differing structural, chemical, physical, and biological properties. The instant application discloses only one species encompassed by the claimed genus which is an isolated polynucleotide consisting of SEQ ID NO: 2 which is disclosed as encoding a myosin homolog having the amino acid sequence of SEQ ID NO: 1. The specification fails to describe additional representative species of the claimed genus. The specification does not provide a written description all the polynucleotides as encompassed by the claimed genus and their biological functions which have yet to be discovered. In absence of any recitation

of function in the claims, one of skill in the art cannot determine which polynucleotides are or are not described by the specification.

The claims of the instant application differ from the claims of the Lilly and Fiers cases in that the claims of the instant application recite a specific nucleotide sequence (SEQ ID NO: 2) and a specific amino acid sequence (SEQ ID NO: 1) while the claims of the Lilly and Fiers cases as reported by the Appellants recite no specific nucleotide of amino acid sequence but rather a nucleic acid encoding a specific protein. A description of the claimed genus of polynucleotides may be achieved by a recitation of a representative number of polynucleotides falling within the scope of the genus. Alternatively, description of the claimed genus of polynucleotides may be achieved by recitation of a correlation of structural features to functional properties that are common to the members of the genus. However, the instant claims do not recite any structure to function correlation and the specification only discloses one member of the claimed genus which is the nucleotide sequence of SEQ ID NO: 2.

Appellants' argument that in view of the Brenner et al. reference the claims do not define a highly variant genus but rather a genus of narrow scope is not persuasive since the claims do not recite the limitation that the claimed polynucleotide has 70% identity to SEQ ID NO: 2 and encode a myosin protein. The Examiner's position regarding the Brenner et al. reference is that it provides an analysis of how to estimate and assign evolutionary homology and functional homology to polypeptides by comparing amino acid sequences, and that the Brenner et al. reference does not teach

when polynucleotides are or are not members of the claimed genus of the instant invention.

While Appellants' statement that the state of the art has advanced since the time of filing of the cited cases of Lilly and Fiers and the present application is valid, it is not apparent that the invention of PCR, efficient cloning and sequencing of DNA, and compilation of large protein and nucleotide sequence databases would enable one of skilled in the art to determine which polynucleotides are or are not described by the specification.

Given the lack of additional representative species as encompassed by the claimed genus, the wide breadth of polynucleotides with widely differing structural, chemical, physical, and biological functions, and the lack of reciting any particular structure to function or activity relationship in the claim; one of skilled in the art would not recognize from the disclosure that Appellants were in possession of the claimed genus of polynucleotides recited in claim 30.

Therefore, for the reasons set forth above, Appellants' arguments and exhibits have been fully and carefully considered, but are not considered sufficient to rebut the prima facie case of lack of utility, enablement, and written description.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

Christian L. Fronda
May 17, 2004

Conferees
Ponnathapura Achutamurthy
SPE, Art Unit 1652

PONNATHAPURA ACHUTAMURTHY
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Michael Wityshyn
SPE, Art Unit 1651

Michael G. Wityshyn (CON FERREE)
Supervisory Patent Examiner
Technology Center 1600

INCYTE CORPORATION (formerly known as Incyte Genomics, Inc.)
3160 PORTER DRIVE
PALO ALTO, CA 94304